In the Specification:

Please amend the specification as shown:

Please delete the paragraph on page 16, line 20, through page 17, line 16, and replace it with the following paragraph:

I. Construction of a universal TIN vector (pTIN511) (Figure 2)

The starting molecule is pTIN500 (described in PCT/GB96/01230). This was derived from pTIN414 described in PCT/GB96/01230 (and described herein in detail below and illustrated in Figure 7). PTin414 is the TIN vector equivalent of retroviral vector PHIT111 (Soneoka *et al* 1995), a derivative of LZSN (Adam *et al* 1991). Subsequent TIN vectors were derived from pTIN414 by replacement of internal sequences between unique SpeI and NheI sites. The SpeI site is located within the non-translated gag coding region upstream of the lacZ gene and the Nhe I site is in the 3' U3 region at the junction of the MLV and HIV-1 sequences. Plasmid pTIN500 contains the SpeI - NheI internal fragment from pBABEpuro. The SV-Puro cassette is deleted by digestion with AccI and religation. This produces pTIN510. A poly-linker is inserted into the unique EcoRI site in pTIN510.

Polylinker sequence ~~(SEQ ID NO: 1)~~

EcoRI SalI XhoI BglII EcoRI

5'AATTCGTCGACCTCGAGATCCG; **(SEQ ID NO: 1)**

GCAGCTGGAGCTCTAGGCAATT 5' **(SEQ ID NO: 2)**

This creates pTIN511 which has unique SalI, XhoI and BglII sites for the insertion of additional sequences.

The removal of the SV-Puro cassette is not critical for the current invention but serves to simplify the structure of the vector. There may be situations,

obvious to one skilled in the area, when the retention of this or any additional cassette might be desirable.

Please delete the paragraph on page 17, line 26, through page 18, line 12, and replace it with the following paragraph:

Plasmid pPE611 (Braddock *et al.* 1989) contains the human CMV promoter (from -521 to +1) joined exactly to the start of the HIV-1 R region (co-ordinates +1 to +80). An XbaI - BamHI fragment from this plasmid was ligated into the cloning vector pBluescript (Stratagene) to give plasmid pRV404. A PCR amplification was performed using plasmid pLNSX as the template, using primers 5'-gcgagctagcttcgaatcgtggtctcgctgttccttgg-3' **(SEQ ID NO: 3)** and 5'ggccgctagcgttcagaactcgtcagttccaccac-3' **(SEQ ID NO:4)**. The PCR product so generated was digested with NheI and ligated into pRV404 at its NheI site to give plasmid pRV405. Two oligonucleotides of sequence 5'-ttaagcctcaataaagcttgccttgagtgcttcatc-3' **(SEQ ID NO: 5)** and 5'- cggatgaagcactcaaggcaagctttattgaggc-3' **(SEQ ID NO: 6)** were annealed together to create a short duplex containing single stranded regions at either end corresponding to the overhangs present on AflII and BstBI restriction fragments. This molecule was ligated into plasmid pRV405 cut with AflII and BstBI, to give plasmid pRV406.

Please delete the paragraph on page 18, lines 14-24, and replace it with the following paragraph:

(ii) Construction of the 3' LTR

A HindIII - XbaI fragment from pLNSX was ligated into the cloning vector pSP72 to give plasmid pRV400. Plasmid pBX+ contains a BamHI - XbaI fragment from WI3 containing the whole 3' LTR from the HIV-1 genome. PCR amplification was performed on pBX+ using primers 5'-ccgcgctagcgatatccttgatctgtggatctaccac-3' **(SEQ ID NO: 7)**

and 5'gcgagggtaccgtcgactgctagagattttccacactgac-3' **(SEQ ID NO:8)**. The PCR product was digested with KpnI and NheI and ligated into plasmid pRV400 digested with KpnI and NheI, to give plasmid pRV401. The ClaI - KpnI fragment of pRV401 was ligated into pBluescript digested with ClaI and KpnI, to give plasmid pRV408.

Please delete the paragraph on page 19, line 21, through page 20, line 12, and replace it with the following paragraph:

4. Construction of pTRAC-TG (Figure 5)

A coding sequence of choice is inserted into one of the unique restriction sites in pTRAC. This sequence is a therapeutic gene or a reporter gene. The sequence is prepared with appropriate restriction at the termini and has an ATG codon for translation initiation. In the present example the RevM10 sequence is amplified from plasmid pM10 (Malim *et al* 1989a) using PCR primers incorporating flanking BglII (upstream) and BamHI (downstream sites).

Primer sequences:

GGCAGATCTATGGCAGGAAGAAGCGG - 3' (SEQ ID NO: ~~2~~ **9**)
GGCGGATCCTTCTTTAGTTCCTGACTCC - 3' (SEQ ID NO: ~~3~~ **10**)

The amplified product is digested with BglI and BamHI and the product is ligated into the unique BglII site of pTRAC. The vector genome is renamed according to the therapeutic gene in this example pTRAC-TG becomes pTRAC-RevM10.

Insertion of the gene in the correct orientation preserves the upstream BglII site but the downstream site is destroyed by the formation of a BglII/BamHI hybrid site.

Please delete the paragraph on page 20, lines 14-29, and replace it with the following paragraph:

5. Construction of pTRIN and pTRIN-TG (Figure 6)

To construct an RRE cassette, a 359 base pair fragment encompassing the minimal fully functional RRE is amplified from pRAC using primers that locate with respect to the HIV proviral sequence coordinates at nucleotide 7705 and 8067 (or from pPE351 sequences from 7707 to 8066). The upstream primer adds an EcoRI site followed by a BamHI site and the downstream primer adds an EcoRI site.

Primer 1 (SEQ ID NO: ~~4~~ **11**) (lower case is HIV-1 sequence 7705 to 7725).
5'CCGCGAATTCGGATCCaggagtagcacccaccaaggc

Primer 2 (SEQ ID NO: ~~5~~ **12**) (lower case is HIV-1 sequence from 8067 to 8047)
5'CCGCGAATTctccaactagcattccaaggc

The amplified product is digested with EoRI and is ligated into the EcoRI site of pTIN510 to produce pTRIN. This now has a unique BamHI site for the insertion of any additional sequences.